Clinical trial results:
Multicenter, randomized, open-label, parallel-group study to evaluate user satisfaction with and tolerability of the low-dose levonorgestrel (LNG) intrauterine delivery system (IUS) with 12 µg LNG/day initial in vitro release rate (LCS12) in comparison to a combined oral contraceptive containing 30 µg ethinyl estradiol and 3 mg drospirenone (Yasmin®) in young nulliparous and parous women (18-29 years) over 18 months of use

Summary

EudraCT number	2010-020181-21
Trial protocol	AT BE DE
Global end of trial date	28 May 2014

Results information

Result version number	v2
This version publication date	04 September 2016
First version publication date	10 May 2015
Version creation reason	• New data added to full data set • Correction of full data set Bayer sponsor contact information to be updated

Trial information

Trial identification

Sponsor protocol code	BAY86-5028/13362

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01254292
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bayer AG
Sponsor organisation address	Kaiser-Wilhelm-Allee, Leverkusen, Germany, D-51368
Public contact	Therapeutic Area Head, Bayer AG, clinical-trials-contact@bayer.com
Scientific contact	Therapeutic Area Head, Bayer AG, clinical-trials-contact@bayer.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Interim
Date of interim/final analysis	08 January 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	08 January 2013
Global end of trial reached?	Yes
Global end of trial date	28 May 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to evaluate user satisfaction in young nulliparous and parous women (18-29 years of age) using LCS12 compared with young nulliparous and parous women using a combined oral contraceptive (COC) over a period of 18 months.

Protection of trial subjects:

The conduct of this clinical study met all local legal and regulatory requirements. The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and the International Conference on Harmonization guideline E6: Good Clinical Practice. Participating subjects signed informed consent form and could withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision. Only investigators qualified by training and experience were selected as appropriate experts to investigate the study drug.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	06 January 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Austria: 173
Country: Number of subjects enrolled	Belgium: 101
Country: Number of subjects enrolled	Germany: 171
Country: Number of subjects enrolled	United States: 122
Worldwide total number of subjects	567
EEA total number of subjects	445

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0

Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	567
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 42 centers in Austria, Belgium, Germany, and the United States in healthy nulliparous and parous women.

Pre-assignment

Screening details:

A total of 644 subjects were screened of which 77 were screen failures and 567 were randomized, as follows: 282 subjects to LCS12 and 285 subjects to Yasmin. 279 subjects received treatment in LCS12 group and 281 in Yasmin group.

Period 1

Period 1 title	Overall trial
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	LCS12 (Jaydess, BAY86-5028)

Arm description:

Subjects received LCS12 for 18 months with optional extension to 36 months.

Arm type	Experimental
Investigational medicinal product name	Levonorgestrel
Investigational medicinal product code	BAY86-5028
Other name	Skyla, Jaydess
Pharmaceutical forms	Intrauterine delivery system
Routes of administration	Intrauterine use

Dosage and administration details:

Subjects received LCS12 for 18 months with optional extension to 36 months.

Arm title	EE30/DRSP (Yasmin, BAY86-5131)

Arm description:

Subjects received COC tablet Yasmin containing 30 microgram ethinyl estradiol (EE) and 3 milligram (mg) drospirenone (DRSP) for 18 months per 19 cycles.

Arm type	Active comparator
Investigational medicinal product name	EE30/DRSP (Yasmin)
Investigational medicinal product code	BAY86-5131
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received COC tablet Yasmin containing 30 microgram EE and 3 mg DRSP for 18 months per 19 cycles.

Number of subjects in period 1	LCS12 (Jaydess, BAY86-5028)	EE30/DRSP (Yasmin, BAY86-5131)
Started	282	285
Subjects Received Treatment	279	281
Completed	227	204
Not completed	55	81
Consent withdrawn by subject	20	21
Wish for pregnancy	4	6
Protocol violation	1	2
Pregnancy	2	6
Adverse event	25	25
Lost to follow-up	3	21

Period 2

Period 2 title	Baseline period
Is this the baseline period?	Yes[1]
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	No
Arm title	LCS12 (Jaydess, BAY86-5028)

Arm description:

Subjects received LCS12 for 18 months with optional extension to 36 months. Subjects who received treatment were included in baseline period.

Arm type	Experimental
Investigational medicinal product name	Levonorgestrel
Investigational medicinal product code	BAY86-5028
Other name	Skyla, Jaydess
Pharmaceutical forms	Intrauterine delivery system
Routes of administration	Intrauterine use

Dosage and administration details:

Subjects received LCS12 for 18 months with optional extension to 36 months.

Arm title	EE30/DRSP (Yasmin, BAY86-5131)

Arm description:

Subjects received COC tablet Yasmin containing 30 microgram EE and 3 mg DRSP for 18 months per 19 cycles. Subjects who received treatment were included in baseline period.

Arm type	Active comparator
Investigational medicinal product name	EE30/DRSP (Yasmin)
Investigational medicinal product code	BAY86-5131
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received COC tablet Yasmin containing 30 microgram EE and 3 mg DRSP for 18 months per 19

cycles.

Notes:

[1] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: In overall trial, all subjects who were randomized were included and the baseline characteristics were provided only for subjects who were treated. Hence, the baseline period of treated subjects was created to publish the baseline characteristics data.

Number of subjects in period 2	LCS12 (Jaydess, BAY86-5028)	EE30/DRSP (Yasmin, BAY86-5131)
Started	279	281
Completed	279	281

Baseline characteristics

Reporting groups[1]	
Reporting group title	LCS12 (Jaydess, BAY86-5028)
Reporting group description:	
Subjects received LCS12 for 18 months with optional extension to 36 months. Subjects who received treatment were included in baseline period.	
Reporting group title	EE30/DRSP (Yasmin, BAY86-5131)
Reporting group description:	
Subjects received COC tablet Yasmin containing 30 microgram EE and 3 mg DRSP for 18 months per 19 cycles. Subjects who received treatment were included in baseline period.	

Notes:

[1] - The number of subjects reported to be in the baseline period is not equal to the worldwide number of subjects enrolled in the trial. It is expected that these numbers will be the same.
Justification: Not all randomized subjects were treated with study drugs. Hence, the worldwide number enrolled in the trial, which is the same as the number randomized, differs from the number of subjects reported in the baseline period.

Reporting group values	LCS12 (Jaydess, BAY86-5028)	EE30/DRSP (Yasmin, BAY86-5131)	Total
Number of subjects	279	281	560
Age categorical Units: Subjects			
Adults (18-64 years)	279	281	560
Age continuous Units: years			
arithmetic mean	23.7	23.9	
standard deviation	± 3	± 3	-
Gender categorical Units: Subjects			
Female	279	281	560
Number of births Units: Subjects			
Zero	216	206	422
One	39	49	88
Two	19	24	43
Three	4	2	6
Four	1	0	1

End points

End points reporting groups

Reporting group title	LCS12 (Jaydess, BAY86-5028)
Reporting group description:	
Subjects received LCS12 for 18 months with optional extension to 36 months.	
Reporting group title	EE30/DRSP (Yasmin, BAY86-5131)
Reporting group description:	
Subjects received COC tablet Yasmin containing 30 microgram ethinyl estradiol (EE) and 3 milligram (mg) drospirenone (DRSP) for 18 months per 19 cycles.	
Reporting group title	LCS12 (Jaydess, BAY86-5028)
Reporting group description:	
Subjects received LCS12 for 18 months with optional extension to 36 months. Subjects who received treatment were included in baseline period.	
Reporting group title	EE30/DRSP (Yasmin, BAY86-5131)
Reporting group description:	
Subjects received COC tablet Yasmin containing 30 microgram EE and 3 mg DRSP for 18 months per 19 cycles. Subjects who received treatment were included in baseline period.	
Subject analysis set title	Full analysis set (FAS)
Subject analysis set type	Full analysis
Subject analysis set description:	
The FAS included all randomized subjects who received treatment (i.e., who took at least one tablet of Yasmin or who had a successful or unsuccessful insertion attempt of LCS12). All subjects in the FAS were analyzed according to the treatment they actually received. The FAS population comprised of 560 subjects, including 279 subjects randomized to LCS12 and 281 subjects randomized to Yasmin.	

Primary: Overall Satisfaction Rate at 18 Months (Last Observation Carried Forward, LOCF)

End point title	Overall Satisfaction Rate at 18 Months (Last Observation Carried Forward, LOCF)[1]
End point description:	
Satisfaction was to be assessed by the subject based on a 5-point Likert item, using the following question: How satisfied are you with the birth control method used during the study? 1. Very satisfied 2. Satisfied 3. Neither satisfied nor dissatisfied 4. Dissatisfied 5. Very dissatisfied. The overall satisfaction rate is the percentage of subjects selecting "1. Very satisfied" or "2. Satisfied" for the above question.	
End point type	Primary
End point timeframe:	
At 18 months	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical analysis was not performed since descriptive statistical analysis was only planned for this endpoint.

End point values	LCS12 (Jaydess, BAY86-5028)	EE30/DRSP (Yasmin, BAY86-5131)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	274[2]	260[3]		
Units: percentage of subjects				
number (confidence interval 95%)	82.1 (77.1 to 86.5)	81.9 (76.7 to 86.4)		

Notes:

[2] - FAS (only subjects with at least one assessment of the overall satisfaction rating)

[3] - FAS (only subjects with at least one assessment of the overall satisfaction rating)

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Satisfaction Rating by the 5-Point Likert Item at 6 Months

End point title	Overall Satisfaction Rating by the 5-Point Likert Item at 6 Months

End point description:

Satisfaction was to be assessed by the subject based on a 5-point Likert item, using the following question: How satisfied are you with the birth control method used during the study? 1. Very satisfied 2. Satisfied 3. Neither satisfied nor dissatisfied 4. Dissatisfied 5. Very dissatisfied The overall satisfaction rate was to be the percentage of subjects selecting "1. Very satisfied" or "2. Satisfied" for the above question.

End point type	Secondary

End point timeframe:

At 6 months

End point values	LCS12 (Jaydess, BAY86-5028)	EE30/DRSP (Yasmin, BAY86-5131)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	273[4]	260[5]		
Units: percentage of subjects				
number (not applicable)				
Very Satisfied	60.4	48.1		
Satisfied	27.5	35.8		
Neither satisfied nor dissatisfied	7.3	9.6		
Dissatisfied	1.8	6.2		
Very Dissatisfied	2.9	0.4		

Notes:

[4] - FAS (only subjects with an assessment of overall satisfaction rating at 6 months)

[5] - FAS (only subjects with an assessment of overall satisfaction rating at 6 months)

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Satisfaction Rating by the 5-Point Likert Item at 12 Months

End point title	Overall Satisfaction Rating by the 5-Point Likert Item at 12 Months

End point description:

Satisfaction was to be assessed by the subject based on a 5-point Likert item, using the following question: How satisfied are you with the birth control method used during the study? 1. Very satisfied 2. Satisfied 3. Neither satisfied nor dissatisfied 4. Dissatisfied 5. Very dissatisfied The overall satisfaction rate was to be the percentage of subjects selecting "1. Very satisfied" or "2. Satisfied" for the above question.

End point type	Secondary
End point timeframe:	
At 12 months	

End point values	LCS12 (Jaydess, BAY86-5028)	EE30/DRSP (Yasmin, BAY86-5131)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	253[6]	238[7]		
Units: percentage of subjects				
number (not applicable)				
Very Satisfied	66.8	45		
Satisfied	22.9	44.1		
Neither satisfied nor dissatisfied	5.9	5.9		
Dissatisfied	4.3	3.8		
Very Dissatisfied	0	1.3		

Notes:

[6] - FAS (only subjects with an assessment of overall satisfaction rating at 12 months)

[7] - FAS (only subjects with an assessment of overall satisfaction rating at 12 months)

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Satisfaction Rating by the 5-Point Likert Item at 18 Months

End point title	Overall Satisfaction Rating by the 5-Point Likert Item at 18 Months

End point description:

Satisfaction was to be assessed by the subject based on a 5-point Likert item, using the following question: How satisfied are you with the birth control method used during the study? 1. Very satisfied 2. Satisfied 3. Neither satisfied nor dissatisfied 4. Dissatisfied 5. Very dissatisfied. The overall satisfaction rate was to be the percentage of subjects selecting "1. Very satisfied" or "2. Satisfied" for the above question.

End point type	Secondary
End point timeframe:	
At 18 months	

End point values	LCS12 (Jaydess, BAY86-5028)	EE30/DRSP (Yasmin, BAY86-5131)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	235[8]	217[9]		
Units: percentage of subjects				
number (not applicable)				
Very Satisfied	64.3	52.5		
Satisfied	25.1	37.8		
Neither satisfied nor dissatisfied	6.4	6.9		
Dissatisfied	3	2.8		
Very Dissatisfied	1.3	0		

Notes:

[8] - FAS (only subjects with an assessment of overall satisfaction rating at 18 months)

[9] - FAS (only subjects with an assessment of overall satisfaction rating at 18 months)

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Satisfaction Rating by the 5-Point Likert Item at End of Study (EOS)

End point title	Overall Satisfaction Rating by the 5-Point Likert Item at End of Study (EOS)

End point description:

Satisfaction was to be assessed by the subject based on a 5-point Likert item, using the following question: How satisfied are you with the birth control method used during the study? 1. Very satisfied 2. Satisfied 3. Neither satisfied nor dissatisfied 4. Dissatisfied 5. Very dissatisfied The overall satisfaction rate was to be the percentage of subjects selecting "1. Very satisfied" or "2. Satisfied" for the above question.

End point type	Secondary

End point timeframe:

At 18 months/EOS

End point values	LCS12 (Jaydess, BAY86-5028)	EE30/DRSP (Yasmin, BAY86-5131)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	268[10]	251[11]		
Units: percentage of subjects				
number (not applicable)				
Very Satisfied	58.6	46.6		
Satisfied	23.5	35.1		
Neither satisfied nor dissatisfied	8.6	9.6		
Dissatisfied	5.6	7.6		
Very Dissatisfied	3.7	1.2		

Notes:

[10] - FAS (only subjects with an assessment of overall satisfaction rating at 18 months/EOS)

[11] - FAS (only subjects with an assessment of overall satisfaction rating at 18 months/EOS)

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Satisfaction Rate at 6 Months (LOCF)

End point title	Overall Satisfaction Rate at 6 Months (LOCF)

End point description:

Satisfaction was to be assessed by the subject based on a 5-point Likert item, using the following question: How satisfied are you with the birth control method used during the study? 1. Very satisfied 2. Satisfied 3. Neither satisfied nor dissatisfied 4. Dissatisfied 5. Very dissatisfied. The overall satisfaction rate was to be the percentage of subjects selecting "1. Very satisfied" or "2. Satisfied" for the above question.

End point type	Secondary

End point timeframe:

At 6 months

End point values	LCS12 (Jaydess, BAY86-5028)	EE30/DRSP (Yasmin, BAY86-5131)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	273[12]	260[13]		
Units: percentage of subjects				
number (not applicable)	87.9	83.8		

Notes:

[12] - FAS (only subjects with an assessment of overall satisfaction rating at 6 months or before)

[13] - FAS (only subjects with an assessment of overall satisfaction rating at 6 months or before)

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Satisfaction Rate at 12 Months (LOCF)

End point title	Overall Satisfaction Rate at 12 Months (LOCF)

End point description:

Satisfaction was to be assessed by the subject based on a 5-point Likert item, using the following question: How satisfied are you with the birth control method used during the study? 1. Very satisfied 2. Satisfied 3. Neither satisfied nor dissatisfied 4. Dissatisfied 5. Very dissatisfied. The overall satisfaction rate was to be the percentage of subjects selecting "1. Very satisfied" or "2. Satisfied" for the above question.

End point type	Secondary

End point timeframe:

At 12 months

End point values	LCS12 (Jaydess, BAY86-5028)	EE30/DRSP (Yasmin, BAY86-5131)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	274[14]	260[15]		
Units: percentage of subjects				
number (not applicable)	84.3	83.8		

Notes:

[14] - FAS (only subjects with an assessment of overall satisfaction rating at 12 months)

[15] - FAS (only subjects with an assessment of overall satisfaction rating at 12 months)

Statistical analyses

No statistical analyses for this end point

Secondary: User Satisfaction – Acceptability of the Administration of Study Treatment

End point title	User Satisfaction – Acceptability of the Administration of Study

	Treatment

End point description:

The degree of user satisfaction was assessed at the end-of-study visit using an eight item questionnaire. One of the items assessed was acceptability of study treatment which was categorized into the following: acceptable without inconvenience/discomfort (I/D), acceptable with some I/D, not acceptable with moderate I/D, and not acceptable with extreme I/D.

End point type	Secondary

End point timeframe:

At 18 months/EOS

End point values	LCS12 (Jaydess, BAY86-5028)	EE30/DRSP (Yasmin, BAY86-5131)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	263[16]	250[17]		
Units: subjects				
Acceptable without I/D	153	186		
Acceptable with some I/D	87	46		
Not acceptable with moderate I/D	11	15		
Not acceptable with extreme I/D	12	3		

Notes:

[16] - FAS (only subjects with an assessment of these questions of the user satisfaction questionnaire)

[17] - FAS (only subjects with an assessment of these questions of the user satisfaction questionnaire)

Statistical analyses

No statistical analyses for this end point

Secondary: User Satisfaction – Choices Upon Completion of the Study

End point title	User Satisfaction – Choices Upon Completion of the Study

End point description:

End point type	Secondary

End point timeframe:

At 18 months/EOS

End point values	LCS12 (Jaydess, BAY86-5028)	EE30/DRSP (Yasmin, BAY86-5131)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	263[18]	248[19]		
Units: subjects				
Continue with study treatment	174	122		
Use a different hormonal contraceptive	34	51		
Use a different contraceptive method	17	27		
Discontinue use of all types of contraceptive	6	14		
No need for contraceptive at this time	5	12		
Undecided	27	22		

Notes:
[18] - FAS (only subjects with an assessment of these questions of the user satisfaction questionnaire)
[19] - FAS (only subjects with an assessment of these questions of the user satisfaction questionnaire)

Statistical analyses

No statistical analyses for this end point

Secondary: User Satisfaction – Amount of Menstrual Bleeding

End point title	User Satisfaction – Amount of Menstrual Bleeding

End point description:

End point type	Secondary

End point timeframe:
At 18 months/EOS

End point values	LCS12 (Jaydess, BAY86-5028)	EE30/DRSP (Yasmin, BAY86-5131)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	260[20]	250[21]		
Units: subjects				
Decreased	80	35		
Not Changed	163	207		
Increased	17	8		

Notes:
[20] - FAS (only subjects with an assessment of these questions of the user satisfaction questionnaire)
[21] - FAS (only subjects with an assessment of these questions of the user satisfaction questionnaire)

Statistical analyses

No statistical analyses for this end point

Secondary: User Satisfaction – Satisfaction With Menstrual Bleeding Pattern

End point title	User Satisfaction – Satisfaction With Menstrual Bleeding Pattern

End point description:

End point type	Secondary

End point timeframe:
At 18 months/EOS

End point values	LCS12 (Jaydess, BAY86-5028)	EE30/DRSP (Yasmin, BAY86-5131)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	263[22]	250[23]		
Units: subjects				
Very satisfied	101	91		
Somewhat satisfied	65	84		
Neither satisfied nor dissatisfied	48	68		
Dissatisfied	19	4		
Very dissatisfied	10	1		
Not applicable	20	2		

Notes:

[22] - FAS (only subjects with an assessment of these questions of the user satisfaction questionnaire)

[23] - FAS (only subjects with an assessment of these questions of the user satisfaction questionnaire)

Statistical analyses

No statistical analyses for this end point

Secondary: User Satisfaction – Frequency of Experiencing Unexpected Bleeding

End point title	User Satisfaction – Frequency of Experiencing Unexpected Bleeding

End point description:

End point type	Secondary

End point timeframe:

At 18 months/EOS

End point values	LCS12 (Jaydess, BAY86-5028)	EE30/DRSP (Yasmin, BAY86-5131)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	263[24]	250[25]		
Units: subjects				
Never	145	219		
Seldom	92	25		
Often	17	5		
Very Often	9	1		

Notes:

[24] - FAS (only subjects with an assessment of these questions of the user satisfaction questionnaire)

[25] - FAS (only subjects with an assessment of these questions of the user satisfaction questionnaire)

Statistical analyses

No statistical analyses for this end point

Secondary: User Satisfaction – Satisfaction With Menstrual Bleeding Absence

End point title	User Satisfaction – Satisfaction With Menstrual Bleeding Absence

End point description:

End point type	Secondary

End point timeframe:

At 18 months/EOS

End point values	LCS12 (Jaydess, BAY86-5028)	EE30/DRSP (Yasmin, BAY86-5131)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	130[26]	14[27]		
Units: subjects				
Very satisfied	96	6		
Somewhat satisfied	18	0		
Neither satisfied nor dissatisfied	14	8		
Dissatisfied	1	0		
Very dissatisfied	1	0		

Notes:

[26] - FAS (only subjects with an assessment of this questions of the user satisfaction questionnaire)

[27] - FAS (only subjects with an assessment of this questions of the user satisfaction questionnaire)

Statistical analyses

No statistical analyses for this end point

Secondary: User Satisfaction – Comparison of Menstrual Pain Intensity Between Now and Before Treatment

End point title	User Satisfaction – Comparison of Menstrual Pain Intensity Between Now and Before Treatment

End point description:

End point type	Secondary

End point timeframe:

At 18 months/EOS

End point values	LCS12 (Jaydess, BAY86-5028)	EE30/DRSP (Yasmin, BAY86-5131)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	259[28]	247[29]		
Units: subjects				
Decreased	118	61		
Not changed	102	169		
Increased	39	17		

Notes:

[28] - FAS (only subjects with an assessment of this questions of the user satisfaction questionnaire)

[29] - FAS (only subjects with an assessment of this questions of the user satisfaction questionnaire)

Statistical analyses

No statistical analyses for this end point

Secondary: User Satisfaction – Rating of Usual Menstrual Pain Intensity

End point title	User Satisfaction – Rating of Usual Menstrual Pain Intensity

End point description:

End point type	Secondary

End point timeframe:

At 18 months/EOS

End point values	LCS12 (Jaydess, BAY86-5028)	EE30/DRSP (Yasmin, BAY86-5131)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	261[30]	249[31]		
Units: subjects				
None	124	82		
Mild	78	92		
Moderate	43	67		
Severe	16	8		

Notes:

[30] - FAS (only subjects with an assessment of these questions of the user satisfaction questionnaire)

[31] - FAS (only subjects with an assessment of these questions of the user satisfaction questionnaire)

Statistical analyses

No statistical analyses for this end point

Secondary: EVAPIL-R Scores at Screening - Composite Score

End point title	EVAPIL-R Scores at Screening - Composite Score

End point description:

The EVAPIL-R scale is a self-questionnaire aimed to assess tolerability of oral contraceptives. A composite score was derived from 16 items and the ratings for presence/absence (rated as 1/0), frequency (rated with values from 0 to 2), intensity (rated from 1 to 3) and bother (rated from 1 to 4) for each item. To calculate the composite score, the bother rating of each item was multiplied by an item- specific multiplier and a weight. Range is 0-12, with higher values indicating more severe symptoms/less tolerability.

End point type	Secondary

End point timeframe:

At screening

End point values	LCS12 (Jaydess, BAY86-5028)	EE30/DRSP (Yasmin, BAY86-5131)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	273[32]	275[33]		
Units: scores on a scale				
arithmetic mean (standard deviation)	0.9386 (± 0.8036)	0.8846 (± 0.8231)		

Notes:

[32] - FAS (subjects with an assessment of the EVAPIL questionnaire where this score could be calculated)
[33] - FAS (subjects with an assessment of the EVAPIL questionnaire where this score could be calculated)

Statistical analyses

No statistical analyses for this end point

Secondary: EVAPIL-R Scores at Screening - Bother Score

End point title	EVAPIL-R Scores at Screening - Bother Score

End point description:

The EVAPIL-R scale is a self-questionnaire aimed to assess tolerability of oral contraceptives. A composite score was derived from 16 items and the ratings for presence/absence (rated as 1/0), frequency (rated with values from 0 to 2), intensity (rated from 1 to 3) and bother (rated from 1 to 4) for each item. To calculate the composite score, the bother rating of each item was multiplied by an item- specific multiplier and a weight. Range is 0-12, with higher values indicating more severe symptoms/less tolerability.

End point type	Secondary

End point timeframe:

At screening

End point values	LCS12 (Jaydess, BAY86-5028)	EE30/DRSP (Yasmin, BAY86-5131)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	273[34]	276[35]		
Units: scores on a scale				
arithmetic mean (standard deviation)	0.5569 (± 0.4451)	0.5188 (± 0.4406)		

Notes:

[34] - FAS (subjects with an assessment of the EVAPIL questionnaire where bother score could be calculated)
[35] - FAS (subjects with an assessment of the EVAPIL questionnaire where bother score could be calculated)

Statistical analyses

No statistical analyses for this end point

Secondary: EVAPIL-R Scores at 6 Months

End point title	EVAPIL-R Scores at 6 Months

End point description:

The EVAPIL-R scale is a self-questionnaire aimed to assess tolerability of oral contraceptives. A composite score was derived from 16 items and the ratings for presence/absence (rated as 1/0), frequency (rated with values from 0 to 2), intensity (rated from 1 to 3) and bother (rated from 1 to 4)

for each item. To calculate the composite score, the bother rating of each item was multiplied by an item- specific multiplier and a weight. Range is 0-12, with higher values indicating more severe symptoms/less tolerability.

End point type	Secondary

End point timeframe:

At 6 months

End point values	LCS12 (Jaydess, BAY86-5028)	EE30/DRSP (Yasmin, BAY86-5131)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	252[36]	243[37]		
Units: scores on a scale				
arithmetic mean (standard deviation)				
Composite score	1.3187 (± 0.9888)	1.1537 (± 0.9947)		
Bother score	0.7364 (± 0.494)	0.655 (± 0.5148)		

Notes:

[36] - FAS (subjects with an assessment of the EVAPIL questionnaire where this scores could be calculated)
[37] - FAS (subjects with an assessment of the EVAPIL questionnaire where this scores could be calculated)

Statistical analyses

No statistical analyses for this end point

Secondary: EVAPIL-R Scores at 12 Months - Composite Score

End point title	EVAPIL-R Scores at 12 Months - Composite Score

End point description:

The EVAPIL-R scale is a self-questionnaire aimed to assess tolerability of oral contraceptives. A composite score was derived from 16 items and the ratings for presence/absence (rated as 1/0), frequency (rated with values from 0 to 2), intensity (rated from 1 to 3) and bother (rated from 1 to 4) for each item. To calculate the composite score, the bother rating of each item was multiplied by an item- specific multiplier and a weight. Range is 0-12, with higher values indicating more severe symptoms/less tolerability. FAS included only subjects with an assessment of the EVAPIL questionnaire at 12 months where the composite score could be calculated.

End point type	Secondary

End point timeframe:

At 12 months

End point values	LCS12 (Jaydess, BAY86-5028)	EE30/DRSP (Yasmin, BAY86-5131)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	229[38]	218[39]		
Units: scores on a scale				
arithmetic mean (standard deviation)	1.4022 (± 1.0126)	1.0535 (± 0.8698)		

Notes:

[38] - FAS (subjects with an assessment of the EVAPIL questionnaire where this score could be calculated)
[39] - FAS (subjects with an assessment of the EVAPIL questionnaire where this score could be calculated)

Statistical analyses

No statistical analyses for this end point

Secondary: EVAPIL-R Scores at 12 Months - Bother Score

End point title	EVAPIL-R Scores at 12 Months - Bother Score

End point description:

The EVAPIL-R scale is a self-questionnaire aimed to assess tolerability of oral contraceptives. A composite score was derived from 16 items and the ratings for presence/absence (rated as 1/0), frequency (rated with values from 0 to 2), intensity (rated from 1 to 3) and bother (rated from 1 to 4) for each item. To calculate the composite score, the bother rating of each item was multiplied by an item- specific multiplier and a weight. Range is 0-12, with higher values indicating more severe symptoms/less tolerability. FAS included only subjects with an assessment of the EVAPIL questionnaire at 12 months where the bother score could be calculated.

End point type	Secondary

End point timeframe:

At 12 months

End point values	LCS12 (Jaydess, BAY86-5028)	EE30/DRSP (Yasmin, BAY86-5131)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	233	218		
Units: scores on a scale				
arithmetic mean (standard deviation)	0.7789 (± 0.512)	0.6015 (± 0.4663)		

Statistical analyses

No statistical analyses for this end point

Secondary: EVAPIL-R Scores at 18 Months/EOS

End point title	EVAPIL-R Scores at 18 Months/EOS

End point description:

The EVAPIL-R scale is a self-questionnaire aimed to assess tolerability of oral contraceptives. A composite score was derived from 16 items and the ratings for presence/absence (rated as 1/0), frequency (rated with values from 0 to 2), intensity (rated from 1 to 3) and bother (rated from 1 to 4) for each item. To calculate the composite score, the bother rating of each item was multiplied by an item- specific multiplier and a weight. Range is 0-12, with higher values indicating more severe symptoms/less tolerability. FAS included only subjects with an assessment of the EVAPIL questionnaire at 18 months/EOS where the scores could be calculated.

End point type	Secondary

End point timeframe:

At 18 months/EOS

End point values	LCS12 (Jaydess, BAY86-5028)	EE30/DRSP (Yasmin, BAY86-5131)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	260[40]	250[41]		
Units: scores on a scale				
arithmetic mean (standard deviation)				
Composite score	1.4804 (± 1.1926)	1.0246 (± 0.9546)		
Bother score	0.8113 (± 0.5765)	0.5908 (± 0.4836)		

Notes:

[40] - FAS (subjects with an assessment of the EVAPIL questionnaire where this score could be calculated)
[41] - FAS (subjects with an assessment of the EVAPIL questionnaire where this score could be calculated)

Statistical analyses

No statistical analyses for this end point

Secondary: Drop-out Rate

End point title	Drop-out Rate

End point description:

The drop-out rate was the amount of subjects that could not complete the study for various reasons. Overall discontinuation rates were analyzed by Kaplan-Meier analyses and presented as cumulative half-yearly drop-out rates.

End point type	Secondary

End point timeframe:

At 6, 12 and 18 months

End point values	LCS12 (Jaydess, BAY86-5028)	EE30/DRSP (Yasmin, BAY86-5131)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	279[42]	281[43]		
Units: percentage of subjects				
number (not applicable)				
at 6 months	7.53	11.39		
at 12 months	13.26	21.71		
at 18 months	18.64	27.4		

Notes:

[42] - FAS

[43] - FAS

Statistical analyses

No statistical analyses for this end point

Secondary: Pearl Index (PI)

End point title	Pearl Index (PI)

End point description:

The Pearl Index was defined as the number of pregnancies per 100 woman years (WYs). Given the assumption that the number of pregnancies follows a Poisson distribution, the Pearl Index thus is the mean of this distribution.

End point type	Secondary

End point timeframe:

Up to 18 months

End point values	LCS12 (Jaydess, BAY86-5028)	EE30/DRSP (Yasmin, BAY86-5131)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	279[44]	281[45]		
Units: pregnancies per 100 women years				
arithmetic mean (confidence interval 95%)	0.57 (0.07 to 2.05)	1.82 (0.67 to 3.97)		

Notes:

[44] - FAS

[45] - FAS

Statistical analyses

No statistical analyses for this end point

Secondary: Compliance Rate for Yasmin Pill Intake

End point title	Compliance Rate for Yasmin Pill Intake

End point description:

End point type	Secondary

End point timeframe:

Up to 18 months

End point values	EE30/DRSP (Yasmin, BAY86-5131)			
Subject group type	Reporting group			
Number of subjects analysed	281[46]			
Units: percentage of subjects				
number (not applicable)				
Missing	2.8			
Compliance <=75%	2.1			
Compliance >75%	95			

Notes:

[46] - FAS

Statistical analyses

No statistical analyses for this end point

Secondary: User Satisfaction – Acceptability of the Administration of Study Treatment

End point title	User Satisfaction – Acceptability of the Administration of Study Treatment

End point description:

The degree of user satisfaction was assessed at the end-of-study visit using an eight item questionnaire. One of the items assessed was acceptability of study treatment which was categorized into the following: acceptable without I/D, acceptable with some I/D, not acceptable with moderate I/D, and not acceptable with extreme I/D.

End point type	Secondary

End point timeframe:

At 6 months

End point values	LCS12 (Jaydess, BAY86-5028)	EE30/DRSP (Yasmin, BAY86-5131)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	256[47]	244[48]		
Units: subjects				
Acceptable without I/D	163	192		
Acceptable with some I/D	87	48		
Not acceptable with moderate I/D	4	4		
Not acceptable with extreme I/D	2	0		

Notes:

[47] - FAS (only subjects with an assessment of these questions of the user satisfaction questionnaire)

[48] - FAS (only subjects with an assessment of these questions of the user satisfaction questionnaire)

Statistical analyses

No statistical analyses for this end point

Secondary: User Satisfaction – Acceptability of the Administration of Study Treatment

End point title	User Satisfaction – Acceptability of the Administration of Study Treatment

End point description:

The degree of user satisfaction was assessed at the end-of-study visit using an eight item questionnaire. One of the items assessed was acceptability of study treatment which was categorized into the following: acceptable without I/D, acceptable with some I/D, not acceptable with moderate I/D, and not acceptable with extreme I/D.

End point type	Secondary

End point timeframe:

At 12 months

End point values	LCS12 (Jaydess, BAY86-5028)	EE30/DRSP (Yasmin, BAY86-5131)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	237[49]	220[50]		
Units: subjects				
Acceptable without I/D	152	185		
Acceptable with some I/D	74	33		
Not acceptable with moderate I/D	9	2		
Not acceptable with extreme I/D	1	0		

Notes:

[49] - FAS (only subjects with an assessment of these questions of the user satisfaction questionnaire)

[50] - FAS (only subjects with an assessment of these questions of the user satisfaction questionnaire)

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Subjects With Partial or Total Expulsion

End point title	Number of Subjects With Partial or Total Expulsion

End point description:

Total expulsion is confirmed if the IUS is observed in the vagina, the IUS is not shown in the uterine cavity by ultrasound, and / or the subject confirms that the system was expelled. Partial expulsion is diagnosed if the IUS can be partially seen in the vagina or is displaced in the cervical canal.

End point type	Other pre-specified

End point timeframe:

Up to 18 months

End point values	LCS12 (Jaydess, BAY86-5028)			
Subject group type	Reporting group			
Number of subjects analysed	279[51]			
Units: subjects				
Partial expulsion	0			
Total expulsion	0			

Notes:

[51] - FAS

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Investigator's Evaluation of Successful IUS Insertion Procedure

End point title	Investigator's Evaluation of Successful IUS Insertion Procedure

End point description:

End point type	Other pre-specified

End point timeframe:

Up to 18 months

End point values	LCS12 (Jaydess, BAY86-5028)			
Subject group type	Reporting group			
Number of subjects analysed	279[52]			
Units: subjects				
Easy	247			
Slightly difficult	31			
Very difficult	1			

Notes:
[52] - FAS

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Subjects' Evaluation of Pain During Successful IUS Insertion Procedure

End point title	Subjects' Evaluation of Pain During Successful IUS Insertion Procedure

End point description:

End point type	Other pre-specified

End point timeframe:
Up to 18 months

End point values	LCS12 (Jaydess, BAY86-5028)			
Subject group type	Reporting group			
Number of subjects analysed	279[53]			
Units: subjects				
None	49			
Mild	125			
Moderate	80			
Severe	25			

Notes:
[53] - FAS

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Investigator's Evaluation of IUS Removal Procedure

End point title	Investigator's Evaluation of IUS Removal Procedure

End point description:

End point type	Other pre-specified

End point timeframe:

Up to 18 months

End point values	LCS12 (Jaydess, BAY86-5028)			
Subject group type	Reporting group			
Number of subjects analysed	76[54]			
Units: subjects				
Missing	2			
Easy	70			
Slightly difficult	3			
Very difficult	1			

Notes:

[54] - FAS (only subjects in the LCS12 arm with documented removal of the IUS)

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Subjects' Evaluation of Pain During IUS Removal Procedure

End point title	Subjects' Evaluation of Pain During IUS Removal Procedure

End point description:

End point type	Other pre-specified

End point timeframe:

Up to 18 months

End point values	LCS12 (Jaydess, BAY86-5028)			
Subject group type	Reporting group			
Number of subjects analysed	76[55]			
Units: subjects				
Missing	3			
None	43			
Mild	24			
Moderate	5			
Severe	1			

Notes:

[55] - FAS (only subjects in the LCS12 arm with documented removal of the IUS)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From start of treatment until 18 months/EOS visit	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	15.1

Reporting groups	
Reporting group title	LCS12 (Jaydess, BAY86-5028)
Reporting group description:	
Subjects received LCS12 for 18 months with optional extension to 36 months.	
Reporting group title	EE30/DRSP (Yasmin, BAY86-5131)
Reporting group description:	
Subjects received COC tablet Yasmin containing 30 microgram EE and 3 mg DRSP for 18 months per 19 cycles.	

Serious adverse events	LCS12 (Jaydess, BAY86-5028)	EE30/DRSP (Yasmin, BAY86-5131)	
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 279 (4.66%)	6 / 281 (2.14%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cervix carcinoma stage 0			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant melanoma			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Incisional hernia			
subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laceration			

subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ligament rupture			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle injury			
subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	1 / 279 (0.36%)	1 / 281 (0.36%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ectopic pregnancy			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Impaired healing			
subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Colitis ulcerative			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral hernia			

subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Cervical dysplasia			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian cyst			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Basedow's disease			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Exostosis			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nose deformity			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 279 (0.36%)	2 / 281 (0.71%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infectious mononucleosis			

subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	LCS12 (Jaydess, BAY86-5028)	EE30/DRSP (Yasmin, BAY86-5131)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	209 / 279 (74.91%)	167 / 281 (59.43%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Anogenital warts			
subjects affected / exposed	2 / 279 (0.72%)	0 / 281 (0.00%)	
occurrences (all)	2	0	
Breast adenoma			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Uterine leiomyoma			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Fibroadenoma of breast			
subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	1	
Vulvovaginal human papilloma virus infection			
subjects affected / exposed	0 / 279 (0.00%)	2 / 281 (0.71%)	
occurrences (all)	0	2	
Vascular disorders			
Haematoma			
subjects affected / exposed	1 / 279 (0.36%)	1 / 281 (0.36%)	
occurrences (all)	1	1	
Hot flush			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Surgical and medical procedures			
Abscess drainage			

subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	1	
Endodontic procedure			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	2	0	
Mole excision			
subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	2	
Mammoplasty			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Tooth extraction			
subjects affected / exposed	2 / 279 (0.72%)	1 / 281 (0.36%)	
occurrences (all)	3	1	
Wisdom teeth removal			
subjects affected / exposed	4 / 279 (1.43%)	1 / 281 (0.36%)	
occurrences (all)	4	1	
Umbilical hernia repair			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	1	
Chronic fatigue syndrome			
subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	1	
Cyst			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Device dislocation			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Discomfort			

subjects affected / exposed	2 / 279 (0.72%)	0 / 281 (0.00%)	
occurrences (all)	2	0	
Fatigue			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Influenza like illness			
subjects affected / exposed	0 / 279 (0.00%)	2 / 281 (0.71%)	
occurrences (all)	0	2	
Irritability			
subjects affected / exposed	3 / 279 (1.08%)	1 / 281 (0.36%)	
occurrences (all)	3	1	
Medical device pain			
subjects affected / exposed	2 / 279 (0.72%)	0 / 281 (0.00%)	
occurrences (all)	4	0	
Malaise			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Oedema peripheral			
subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	1	
Pain			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Pyrexia			
subjects affected / exposed	3 / 279 (1.08%)	2 / 281 (0.71%)	
occurrences (all)	3	2	
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	1	
Hypersensitivity			
subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	1	
Seasonal allergy			
subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	1	

Reproductive system and breast disorders			
Adnexa uteri cyst			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Adnexa uteri pain			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Amenorrhoea			
subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	1	
Bartholin's cyst			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Breast atrophy			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Breast discomfort			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Breast discharge			
subjects affected / exposed	2 / 279 (0.72%)	0 / 281 (0.00%)	
occurrences (all)	3	0	
Breast disorder			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Breast fibrosis			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Breast pain			
subjects affected / exposed	3 / 279 (1.08%)	1 / 281 (0.36%)	
occurrences (all)	3	1	
Breast swelling			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Breast tenderness			

subjects affected / exposed	3 / 279 (1.08%)	2 / 281 (0.71%)	
occurrences (all)	3	2	
Cervix haemorrhage uterine			
subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	1	
Cervical dysplasia			
subjects affected / exposed	25 / 279 (8.96%)	16 / 281 (5.69%)	
occurrences (all)	29	17	
Coital bleeding			
subjects affected / exposed	3 / 279 (1.08%)	1 / 281 (0.36%)	
occurrences (all)	3	1	
Dyspareunia			
subjects affected / exposed	2 / 279 (0.72%)	0 / 281 (0.00%)	
occurrences (all)	2	0	
Dysmenorrhoea			
subjects affected / exposed	45 / 279 (16.13%)	26 / 281 (9.25%)	
occurrences (all)	71	73	
Ectropion of cervix			
subjects affected / exposed	2 / 279 (0.72%)	0 / 281 (0.00%)	
occurrences (all)	2	0	
Endometrial hypertrophy			
subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	1	
Galactorrhoea			
subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	1	
Genital discharge			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Haemorrhagic ovarian cyst			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Genital haemorrhage			
subjects affected / exposed	6 / 279 (2.15%)	0 / 281 (0.00%)	
occurrences (all)	8	0	
Menometrorrhagia			

subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	1	
Menorrhagia			
subjects affected / exposed	5 / 279 (1.79%)	5 / 281 (1.78%)	
occurrences (all)	5	5	
Metrorrhagia			
subjects affected / exposed	9 / 279 (3.23%)	1 / 281 (0.36%)	
occurrences (all)	12	1	
Menstruation irregular			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Nipple pain			
subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	1	
Ovarian cyst			
subjects affected / exposed	19 / 279 (6.81%)	0 / 281 (0.00%)	
occurrences (all)	20	0	
Oligomenorrhoea			
subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	1	
Ovarian cyst ruptured			
subjects affected / exposed	2 / 279 (0.72%)	0 / 281 (0.00%)	
occurrences (all)	2	0	
Ovulation pain			
subjects affected / exposed	2 / 279 (0.72%)	0 / 281 (0.00%)	
occurrences (all)	2	0	
Pelvic discomfort			
subjects affected / exposed	2 / 279 (0.72%)	0 / 281 (0.00%)	
occurrences (all)	2	0	
Pelvic pain			
subjects affected / exposed	12 / 279 (4.30%)	0 / 281 (0.00%)	
occurrences (all)	13	0	
Uterine haemorrhage			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Uterine pain			

subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Vaginal discharge			
subjects affected / exposed	6 / 279 (2.15%)	0 / 281 (0.00%)	
occurrences (all)	6	0	
Vaginal haemorrhage			
subjects affected / exposed	6 / 279 (2.15%)	0 / 281 (0.00%)	
occurrences (all)	6	0	
Vulval haematoma			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Vaginal odour			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Vulvovaginal dryness			
subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	1	
Vulvovaginal pruritus			
subjects affected / exposed	2 / 279 (0.72%)	1 / 281 (0.36%)	
occurrences (all)	2	2	
Vulvovaginal pain			
subjects affected / exposed	1 / 279 (0.36%)	1 / 281 (0.36%)	
occurrences (all)	2	1	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 279 (0.36%)	3 / 281 (1.07%)	
occurrences (all)	1	3	
Dyspnoea			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Oropharyngeal pain			
subjects affected / exposed	5 / 279 (1.79%)	2 / 281 (0.71%)	
occurrences (all)	6	2	
Rhinitis allergic			

subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	1	
Psychiatric disorders			
Affective disorder			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Adjustment disorder			
subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	1	
Anxiety			
subjects affected / exposed	1 / 279 (0.36%)	1 / 281 (0.36%)	
occurrences (all)	1	1	
Depressed mood			
subjects affected / exposed	1 / 279 (0.36%)	1 / 281 (0.36%)	
occurrences (all)	1	1	
Attention deficit/hyperactivity disorder			
subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	1	
Depression			
subjects affected / exposed	1 / 279 (0.36%)	4 / 281 (1.42%)	
occurrences (all)	1	4	
Insomnia			
subjects affected / exposed	0 / 279 (0.00%)	4 / 281 (1.42%)	
occurrences (all)	0	5	
Libido decreased			
subjects affected / exposed	1 / 279 (0.36%)	3 / 281 (1.07%)	
occurrences (all)	1	3	
Loss of libido			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Mood swings			
subjects affected / exposed	0 / 279 (0.00%)	2 / 281 (0.71%)	
occurrences (all)	0	2	
Mood altered			

subjects affected / exposed	1 / 279 (0.36%)	3 / 281 (1.07%)	
occurrences (all)	1	3	
Nervousness			
subjects affected / exposed	1 / 279 (0.36%)	1 / 281 (0.36%)	
occurrences (all)	1	1	
Sleep disorder			
subjects affected / exposed	0 / 279 (0.00%)	2 / 281 (0.71%)	
occurrences (all)	0	2	
Stress			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Investigations			
Blood pressure decreased			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Chlamydia test positive			
subjects affected / exposed	1 / 279 (0.36%)	2 / 281 (0.71%)	
occurrences (all)	1	2	
Body temperature increased			
subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	2	
Gardnerella test positive			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	2	0	
Helicobacter test positive			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Human papilloma virus test positive			
subjects affected / exposed	4 / 279 (1.43%)	3 / 281 (1.07%)	
occurrences (all)	4	3	
Liver function test abnormal			
subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	1	
Smear cervix abnormal			
subjects affected / exposed	5 / 279 (1.79%)	0 / 281 (0.00%)	
occurrences (all)	6	0	

Weight decreased			
subjects affected / exposed	1 / 279 (0.36%)	3 / 281 (1.07%)	
occurrences (all)	1	3	
Weight increased			
subjects affected / exposed	6 / 279 (2.15%)	8 / 281 (2.85%)	
occurrences (all)	6	8	
Injury, poisoning and procedural complications			
Accident			
subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	2	
Animal bite			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Arthropod bite			
subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	1	
Epicondylitis			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Contusion			
subjects affected / exposed	0 / 279 (0.00%)	3 / 281 (1.07%)	
occurrences (all)	0	3	
Humerus fracture			
subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	1	
Joint dislocation			
subjects affected / exposed	2 / 279 (0.72%)	0 / 281 (0.00%)	
occurrences (all)	2	0	
Laceration			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Ligament rupture			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	2	0	
Ligament sprain			

subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	1	
Limb injury			
subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	1	
Muscle strain			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Post procedural complication			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Post procedural discomfort			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Post-traumatic neck syndrome			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Post-traumatic pain			
subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	2	
Procedural pain			
subjects affected / exposed	10 / 279 (3.58%)	1 / 281 (0.36%)	
occurrences (all)	10	2	
Procedural nausea			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Road traffic accident			
subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	1	
Thermal burn			
subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	1	
Stress fracture			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Tooth fracture			

subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Cardiovascular disorder			
subjects affected / exposed	1 / 279 (0.36%)	1 / 281 (0.36%)	
occurrences (all)	1	1	
Palpitations			
subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	1	
Nervous system disorders			
Aphonia psychogenic			
subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	1	
Dizziness			
subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	1	
Epilepsy			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Headache			
subjects affected / exposed	21 / 279 (7.53%)	33 / 281 (11.74%)	
occurrences (all)	72	56	
Hypertonia			
subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	1	
Migraine			
subjects affected / exposed	2 / 279 (0.72%)	5 / 281 (1.78%)	
occurrences (all)	2	11	
Neuritis			
subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	1	
Neuropathy peripheral			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Presyncope			

subjects affected / exposed	2 / 279 (0.72%)	0 / 281 (0.00%)	
occurrences (all)	2	0	
Sciatica			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Syncope			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	1	
Iron deficiency anaemia			
subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	1	
Lymphadenopathy			
subjects affected / exposed	1 / 279 (0.36%)	1 / 281 (0.36%)	
occurrences (all)	1	1	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	3 / 279 (1.08%)	0 / 281 (0.00%)	
occurrences (all)	3	0	
Eye disorders			
Uveitis			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	2	
Abdominal distension			
subjects affected / exposed	2 / 279 (0.72%)	1 / 281 (0.36%)	
occurrences (all)	2	1	
Abdominal pain			
subjects affected / exposed	21 / 279 (7.53%)	4 / 281 (1.42%)	
occurrences (all)	31	5	
Abdominal pain upper			

subjects affected / exposed	3 / 279 (1.08%)	6 / 281 (2.14%)	
occurrences (all)	3	6	
Abdominal pain lower			
subjects affected / exposed	9 / 279 (3.23%)	5 / 281 (1.78%)	
occurrences (all)	16	5	
Colitis ulcerative			
subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	1	
Diarrhoea			
subjects affected / exposed	1 / 279 (0.36%)	9 / 281 (3.20%)	
occurrences (all)	1	11	
Constipation			
subjects affected / exposed	0 / 279 (0.00%)	4 / 281 (1.42%)	
occurrences (all)	0	4	
Dyspepsia			
subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	1	
Gastric mucosa erythema			
subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	1	
Gastrooesophageal reflux disease			
subjects affected / exposed	3 / 279 (1.08%)	3 / 281 (1.07%)	
occurrences (all)	3	3	
Gastritis			
subjects affected / exposed	4 / 279 (1.43%)	4 / 281 (1.42%)	
occurrences (all)	4	5	
Haemorrhoids			
subjects affected / exposed	1 / 279 (0.36%)	1 / 281 (0.36%)	
occurrences (all)	1	1	
Hypoaesthesia oral			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Hiatus hernia			
subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	1	
Nausea			

subjects affected / exposed	9 / 279 (3.23%)	14 / 281 (4.98%)	
occurrences (all)	16	16	
Proctitis			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Toothache			
subjects affected / exposed	3 / 279 (1.08%)	2 / 281 (0.71%)	
occurrences (all)	4	2	
Rectal haemorrhage			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Vomiting			
subjects affected / exposed	3 / 279 (1.08%)	8 / 281 (2.85%)	
occurrences (all)	3	9	
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	30 / 279 (10.75%)	5 / 281 (1.78%)	
occurrences (all)	35	5	
Alopecia			
subjects affected / exposed	2 / 279 (0.72%)	1 / 281 (0.36%)	
occurrences (all)	2	1	
Dermatitis			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Dermatitis contact			
subjects affected / exposed	2 / 279 (0.72%)	0 / 281 (0.00%)	
occurrences (all)	2	0	
Dermatitis acneiform			
subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	1	
Eczema			

subjects affected / exposed	1 / 279 (0.36%)	1 / 281 (0.36%)	
occurrences (all)	2	1	
Hidradenitis			
subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	1	
Hyperhidrosis			
subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	1	
Lichen sclerosus			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Photosensitivity reaction			
subjects affected / exposed	0 / 279 (0.00%)	2 / 281 (0.71%)	
occurrences (all)	0	2	
Psoriasis			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Rash			
subjects affected / exposed	2 / 279 (0.72%)	0 / 281 (0.00%)	
occurrences (all)	2	0	
Seborrhoea			
subjects affected / exposed	2 / 279 (0.72%)	1 / 281 (0.36%)	
occurrences (all)	2	1	
Skin disorder			
subjects affected / exposed	3 / 279 (1.08%)	0 / 281 (0.00%)	
occurrences (all)	3	0	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Nephrolithiasis			
subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	1	
Endocrine disorders			
Autoimmune thyroiditis			

subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Hypothyroidism			
subjects affected / exposed	3 / 279 (1.08%)	2 / 281 (0.71%)	
occurrences (all)	3	2	
Hyperprolactinaemia			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Axillary mass			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Back pain			
subjects affected / exposed	6 / 279 (2.15%)	4 / 281 (1.42%)	
occurrences (all)	6	6	
Fracture pain			
subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	1	
Muscle tightness			
subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	1	
Myalgia			
subjects affected / exposed	2 / 279 (0.72%)	1 / 281 (0.36%)	
occurrences (all)	2	1	
Neck pain			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Synovitis			
subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	1	
Infections and infestations			
Acute tonsillitis			
subjects affected / exposed	4 / 279 (1.43%)	6 / 281 (2.14%)	
occurrences (all)	4	6	
Appendicitis			

subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	1	
Borrelia infection			
subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	1	
Bronchitis			
subjects affected / exposed	4 / 279 (1.43%)	4 / 281 (1.42%)	
occurrences (all)	4	6	
Cellulitis			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Candidiasis			
subjects affected / exposed	2 / 279 (0.72%)	2 / 281 (0.71%)	
occurrences (all)	2	2	
Cervicitis			
subjects affected / exposed	1 / 279 (0.36%)	1 / 281 (0.36%)	
occurrences (all)	1	1	
Chlamydial infection			
subjects affected / exposed	2 / 279 (0.72%)	1 / 281 (0.36%)	
occurrences (all)	2	1	
Conjunctivitis viral			
subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	1	
Cystitis			
subjects affected / exposed	17 / 279 (6.09%)	15 / 281 (5.34%)	
occurrences (all)	20	19	
Diarrhoea infectious			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Endometritis			
subjects affected / exposed	1 / 279 (0.36%)	1 / 281 (0.36%)	
occurrences (all)	1	1	
Enterococcal infection			
subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	1	
Folliculitis			

subjects affected / exposed	2 / 279 (0.72%)	1 / 281 (0.36%)	
occurrences (all)	3	1	
Gardnerella infection			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Fungal infection			
subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	1	
Gastroenteritis			
subjects affected / exposed	2 / 279 (0.72%)	4 / 281 (1.42%)	
occurrences (all)	2	4	
Gastrointestinal viral infection			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Gonorrhoea			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Herpes zoster			
subjects affected / exposed	1 / 279 (0.36%)	1 / 281 (0.36%)	
occurrences (all)	1	1	
Hordeolum			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Impetigo			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Infectious mononucleosis			
subjects affected / exposed	1 / 279 (0.36%)	1 / 281 (0.36%)	
occurrences (all)	1	2	
Influenza			
subjects affected / exposed	2 / 279 (0.72%)	3 / 281 (1.07%)	
occurrences (all)	5	3	
Kidney infection			
subjects affected / exposed	1 / 279 (0.36%)	1 / 281 (0.36%)	
occurrences (all)	1	1	
Laryngitis			

subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Mastitis			
subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	1	
Nasopharyngitis			
subjects affected / exposed	17 / 279 (6.09%)	14 / 281 (4.98%)	
occurrences (all)	29	18	
Otitis media			
subjects affected / exposed	2 / 279 (0.72%)	1 / 281 (0.36%)	
occurrences (all)	2	1	
Papilloma viral infection			
subjects affected / exposed	1 / 279 (0.36%)	1 / 281 (0.36%)	
occurrences (all)	1	1	
Pharyngitis			
subjects affected / exposed	1 / 279 (0.36%)	2 / 281 (0.71%)	
occurrences (all)	1	2	
Pharyngitis streptococcal			
subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	1	
Pneumonia			
subjects affected / exposed	0 / 279 (0.00%)	2 / 281 (0.71%)	
occurrences (all)	0	2	
Pulpitis dental			
subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	1	
Respiratory tract infection			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Pyelonephritis			
subjects affected / exposed	2 / 279 (0.72%)	1 / 281 (0.36%)	
occurrences (all)	3	1	
Respiratory tract infection viral			
subjects affected / exposed	0 / 279 (0.00%)	2 / 281 (0.71%)	
occurrences (all)	0	2	
Rhinitis			

subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	1	
Salpingo-oophoritis			
subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	1	
Salmonellosis			
subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	1	
Scarlet fever			
subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	1	
Sialoadenitis			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Sinusitis			
subjects affected / exposed	2 / 279 (0.72%)	6 / 281 (2.14%)	
occurrences (all)	2	7	
Tonsillitis			
subjects affected / exposed	3 / 279 (1.08%)	4 / 281 (1.42%)	
occurrences (all)	3	5	
Tooth infection			
subjects affected / exposed	0 / 279 (0.00%)	3 / 281 (1.07%)	
occurrences (all)	0	3	
Urinary tract infection			
subjects affected / exposed	11 / 279 (3.94%)	5 / 281 (1.78%)	
occurrences (all)	11	5	
Upper respiratory tract infection			
subjects affected / exposed	2 / 279 (0.72%)	1 / 281 (0.36%)	
occurrences (all)	4	1	
Vaginal infection			
subjects affected / exposed	8 / 279 (2.87%)	7 / 281 (2.49%)	
occurrences (all)	11	8	
Vaginitis bacterial			
subjects affected / exposed	9 / 279 (3.23%)	3 / 281 (1.07%)	
occurrences (all)	9	3	
Vaginitis chlamydial			

subjects affected / exposed	2 / 279 (0.72%)	0 / 281 (0.00%)	
occurrences (all)	2	0	
Vaginitis gardnerella			
subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	1	
Vulval abscess			
subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	1	
Vulvitis			
subjects affected / exposed	3 / 279 (1.08%)	0 / 281 (0.00%)	
occurrences (all)	3	0	
Vulvovaginal candidiasis			
subjects affected / exposed	13 / 279 (4.66%)	7 / 281 (2.49%)	
occurrences (all)	16	8	
Vulvovaginal mycotic infection			
subjects affected / exposed	8 / 279 (2.87%)	7 / 281 (2.49%)	
occurrences (all)	10	7	
Vulvovaginitis			
subjects affected / exposed	2 / 279 (0.72%)	3 / 281 (1.07%)	
occurrences (all)	2	5	
Vulvovaginitis streptococcal			
subjects affected / exposed	3 / 279 (1.08%)	0 / 281 (0.00%)	
occurrences (all)	3	0	
Vulvovaginitis trichomonal			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	1	
Iron deficiency			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	
Lactose intolerance			
subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	1	

Type 2 diabetes mellitus			
subjects affected / exposed	0 / 279 (0.00%)	1 / 281 (0.36%)	
occurrences (all)	0	1	
Vitamin D deficiency			
subjects affected / exposed	1 / 279 (0.36%)	0 / 281 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 March 2011	The extension phase for LCS12 users was added. Several of the original exclusion criteria were clarified under Amendment 1. An 18-month Extension Phase for subjects in the LCS12 treatment group was added. The timing of Visit 2 and switching of subjects from other forms of contraception was modified. Modified the protocol in response to requests from German Health Authority, to state that in Germany, only a gynaecologist may (1) insert the LCS12 and (2) perform gynaecologic investigations and procedures required by the study protocol. The section on withdrawal of subjects from the study was modified to state that subjects experiencing new-onset of migraine with neurological symptoms, thromboembolic diseases during study treatment, icterus or pronounced increase in blood pressured MUST be withdrawn from treatment. The size of ovarian cysts to be reported as AEs from 5 cm to >3 cm was changed. Discontinued collection of dysmenorrhea data in the subjects' diaries.
22 July 2011	The primary endpoint was clarified. Instructions regarding the use of backup contraception by LCS12 subjects who prematurely discontinued the study were modified. Safety follow-up and EOS assessments for subjects who prematurely discontinued the study was clarified. Clarified protocol to ensure that all pregnancies occurring during the study were appropriately reported to the Sponsor, not only those occurring while study drug was being used. Modified the protocol to indicate that the final clinical study report was not to include the results for the assessment of return to fertility as these data would not be available at the time of database closure. Corrected inconsistent information in the protocol regarding the time allowed between the Screening Visit and Treatment-assignment Visit. Changed definition of a compliant cycle in the COC group to indicate that no tablet could be forgotten on Cycle Days 1 through 21 and that the cycle length was to be no more than 28 days.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported